

IN THE CLAIMS:

N.E. already canceled
Please cancel claims 1-17, 29, 43 and 103-104 currently pending in the application without prejudice and enter the following new claims 112-140:

R.1.126
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~~112~~ A method for obtaining tissue information representative of a given tissue type, comprising the steps of:

- cl*
- (A) profiling a sample of tissue specimens of the given tissue type obtained from a subset of a given population of subjects with shared characteristics to generate a given plurality of structural indices;
 - (B) applying a plurality of imaging methods to image a plurality of sections of each tissue specimen in the sample in order to derive imaging information representative of the sample; and
 - (C) reducing the imaging information to the given plurality of structural indices wherein the given plurality of structural indices corresponds to statistically significant representations of tissue characteristics representative of the given tissue type.

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~~113~~ The method of claim ¹³⁵~~112~~, wherein step (A) comprises the steps of:

- (i) determining distributions of cell density values, matrix density values and blood vessel density values associated with the plurality of sections in accordance with the imaging information; and
- (ii) determining a cell density index representative of tissue associated with the population in accordance with the distribution of cell density values determined in step (i); determining a matrix density index representative of tissue associated with the population in accordance with the distribution of matrix density values determined in step (i); and determining a blood vessel density index representative of tissue associated with the population in accordance with the distribution of blood vessel density values determined in step (i).

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~~114~~ The method of claim ¹³⁶~~113~~, wherein step (A)(ii) comprises:

- (ii) determining a cell density index representative of tissue associated with the population by calculating a statistical average of the distribution of cell density values

determined in step (i); determining a matrix density index representative of tissue associated with the population by calculating a statistical average of the distribution of matrix density values determined in step (i); and determining a blood vessel density index representative of tissue associated with the population by calculating a statistical average of the distribution of blood vessel density values determined in step (i).

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115. The method of claim 114, wherein the statistical average of the distribution of cell density values corresponds to a mean, median or mode of the distribution of cell density values, the statistical average of the distribution of matrix density values corresponds to a mean, median or mode of the distribution of matrix density values, and the statistical average of the distribution of blood vessel density values corresponds to a mean, median or mode of the distribution of blood vessel density values.

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116. The method of claim 115, wherein step (A)(ii) further comprises:
(iii) determining a further cell density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of cell density values determined in step (i); determining a further matrix density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of matrix density values determined in step (i); and determining a further blood vessel density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of blood vessel density values determined in step (i).

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117. The method of claim 116, wherein the index of dispersion associated with the distribution of cell density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of cell density values, the index of dispersion associated with the distribution of matrix density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of matrix density values, and the index of dispersion associated with the distribution of blood vessel density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of blood vessel density values.

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~~118.~~ The method of claim ¹³⁹~~117~~, wherein the plurality of structural indices generated in step (A) further include relative cell location, relative matrix location, and relative blood vessel location.

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~~119.~~ The method of claim ¹⁴⁰~~118~~, wherein step (A)(i) further comprises the steps of:
(ii) determining distributions of relative cell location values, relative matrix location values and relative blood vessel location values associated with the plurality of sections in accordance with the imaging information; and
step (A)(ii) further comprises the step of:
(iii) determining a relative cell location index representative of tissue associated with the population in accordance with the distribution of relative cell location values determined in step (ii); determining a relative matrix location index representative of tissue associated with the population in accordance with the distribution of relative matrix location values determined in step (ii); and determining a relative blood vessel location index representative of tissue associated with the population in accordance with the distribution of relative blood vessel location values determined in step (ii).

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~~120.~~ The method of claim ¹⁴¹~~119~~, wherein step (A)(ii) further comprises:
(iii) determining a relative cell location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative cell location values determined in step (i); determining a relative matrix location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative matrix location values determined in step (i); and determining a relative blood vessel location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative blood vessel location values determined in step (i).

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~~121.~~ The method of claim ¹⁴²~~120~~, wherein the statistical average of the distribution of relative cell location values corresponds to a mean, median or mode of the distribution of relative cell location values, the statistical average of the distribution of relative matrix location values

corresponds to a mean, median or mode of the distribution of relative matrix location values, and the statistical average of the distribution of relative blood vessel location values corresponds to a mean, median or mode of the distribution of relative blood vessel location values.

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122. The method of claim ¹⁴³121, wherein step (A)(iii) further comprises:

(iv) determining a further relative cell location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative cell location values determined in step (ii); determining a further relative matrix location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative matrix location values determined in step (i); and determining a further relative blood vessel location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative blood vessel location values determined in step (ii).

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123. The method of claim ¹⁴⁴122, wherein the index of dispersion associated with the distribution of relative cell location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative cell location values, the index of dispersion associated with the distribution of relative matrix location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative matrix location values, and the index of dispersion associated with the distribution of relative blood vessel location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative blood vessel location values.

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124. The method of claim ¹⁴⁵123, wherein the imaging information in step (B) includes coordinates of cells, matrices and blood vessels.

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125. The method of claim ¹⁴⁶124, wherein the coordinates correspond to Cartesian coordinates.

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126. The method of claim ¹⁴⁵123, wherein the imaging information is derived in step (B) using at least one imaging modality selected from the group consisting of light microscopy,

fluorescent microscopy, spectral microscopy, hyper-spectral microscopy, electron microscopy, confocal microscopy and optical coherence tomography.

R.1.12b
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127. The method of claim ¹⁴⁸126, wherein the imaging information is derived in step (B) using a combination of two or more imaging modalities selected from the following group of imaging modalities: light microscopy, fluorescent microscopy, spectral microscopy, hyper-spectral microscopy, electron microscopy, confocal microscopy and optical coherence tomography.

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128. The method of claim ¹⁴⁵123, wherein the subjects with shared characteristics comprise a group of tissue specimens associated with specific race, sex, age, presence of disease, absence of disease, stage of disease, physical fitness level, behavior, geographic location or nationality of persons.

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129. The method of claim ¹⁴⁵123, wherein step (A) further comprises profiling the sample of tissue specimens to generate one or more mechanical indices wherein the mechanical indices corresponds to statistically significant representations of tissue characteristics representative of the given tissue type.

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130. The method of claim ¹⁴⁵123, wherein step (A) further comprises performing a plurality of cell function assays on the sample of tissue specimens to generate a given plurality of cell function indices and reducing the assay information to the given plurality of cell function indices, wherein the given plurality of cell function indices corresponds to statistically significant representations of tissue characteristics representative of the given tissue type.

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131. A method for obtaining tissue information representative of a given tissue type, comprising the steps of:

(A) performing a plurality of cell function assays on a sample of tissue specimens of the given tissue type obtained from a subset of a given population of subjects with shared characteristics to generate a given plurality of cell function indices;

(B) deriving assay information representative of each tissue specimen in the sample; and

(C) reducing the assay information to the given plurality of cell function indices wherein the given plurality of cell function indices corresponds to statistically significant representations of tissue characteristics representative of the given tissue type.

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132. The method of claim 131, wherein step (A) further comprises forming a cell function map in accordance with the cell function indices.

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133. A method for obtaining imaging information representative of a given tissue type, comprising:

(A) profiling a sample of tissue specimens of the given tissue type obtained from a subset of a given population of subjects with shared characteristics to generate a given plurality of structural indices that corresponds to statistically significant representations of tissue characteristics representative of the given tissue type; and

(B) applying a plurality of imaging methods to image a plurality of sections of each tissue specimen in the sample in order to derive imaging information representative of the sample.

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134. The method of claim 133, wherein step (A) comprises the step of determining distributions of cell density values, matrix density values and blood vessel density values associated with the plurality of sections in accordance with the imaging information.

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135. A method for manufacturing engineered tissue, comprising the steps of:

(A) profiling a sample of normal tissue specimens obtained from a subset of a population of subjects with shared characteristics to generate a plurality of structural indices that correspond to statistically significant representations of characteristics of tissue associated with the population, wherein the plurality of structural indices include cell density, matrix density, blood vessel density and layer thickness;

(B) forming an engineered tissue design in accordance with the structural indices generated in step (A); and

(C) manufacturing engineered tissue in accordance with the engineered tissue design.

R.1.126 ¹⁵⁸
136. The method of claim 1, wherein step (A) comprises the steps of:

(i) deriving imaging information by imaging a plurality of sections of each tissue specimen from the subset;

(ii) determining distributions of cell density values, matrix density values and blood vessel density values associated with the plurality of sections in accordance with the imaging information; and

(iii) determining a cell density index representative of tissue associated with the population in accordance with the distribution of cell density values determined in step (i); determining a matrix density index representative of tissue associated with the population in accordance with the distribution of matrix density values determined in step (ii); and determining a blood vessel density index representative of tissue associated with the population in accordance with the distribution of blood vessel density values determined in step (ii).

¹⁵⁹137. The method of claim 2, wherein step (A)(iii) comprises:

(ii) determining a cell density index representative of tissue associated with the population by calculating a statistical average of the distribution of cell density values determined in step (i); determining a matrix density index representative of tissue associated with the population by calculating a statistical average of the distribution of matrix density values determined in step (ii); and determining a blood vessel density index representative of tissue associated with the population by calculating a statistical average of the distribution of blood vessel density values determined in step (ii).

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138. The method of claim 3, wherein the statistical average of the distribution of cell density values corresponds to a mean, median or mode of the distribution of cell density values, the statistical average of the distribution of matrix density values corresponds to a mean, median or mode of the distribution of matrix density values, and the statistical average of the distribution of blood vessel density values corresponds to a mean, median or mode of the distribution of blood vessel density values.

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139. The method of claim 4, wherein step (A)(iii) further comprises:

(iii) determining a further cell density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of cell density values determined in step (ii); determining a further matrix density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of matrix density values determined in step (ii); and determining a further blood vessel density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of blood vessel density values determined in step (ii).

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140. A method for manufacturing engineered tissue, comprising the steps of:

(A) performing a plurality of cell function assays on a sample of normal tissue specimens obtained from a subset of the population of subjects with shared characteristics and generating a plurality of cell function indices that correspond to statistically significant representations of characteristics of tissue associated with the population in accordance with results of the cell function assays;

(B) forming an engineered tissue design in accordance with the cell function indices; and

(C) manufacturing engineered tissue in accordance with the engineered tissue design.

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